

THE EFFECT OF MATERNAL PERTUSSIS IMMUNIZATION ON INFANT

Dr. Trần Ngọc Xuân

Content

- Overview of pertussis disease
- The effect of maternal pertussis immunization on infant
- The safety of pertussis vaccination in pregnant women
- Optimal time for vaccination

Pertussis Disease

Pertussis is a highly contagious and potentially serious respiratory disease¹

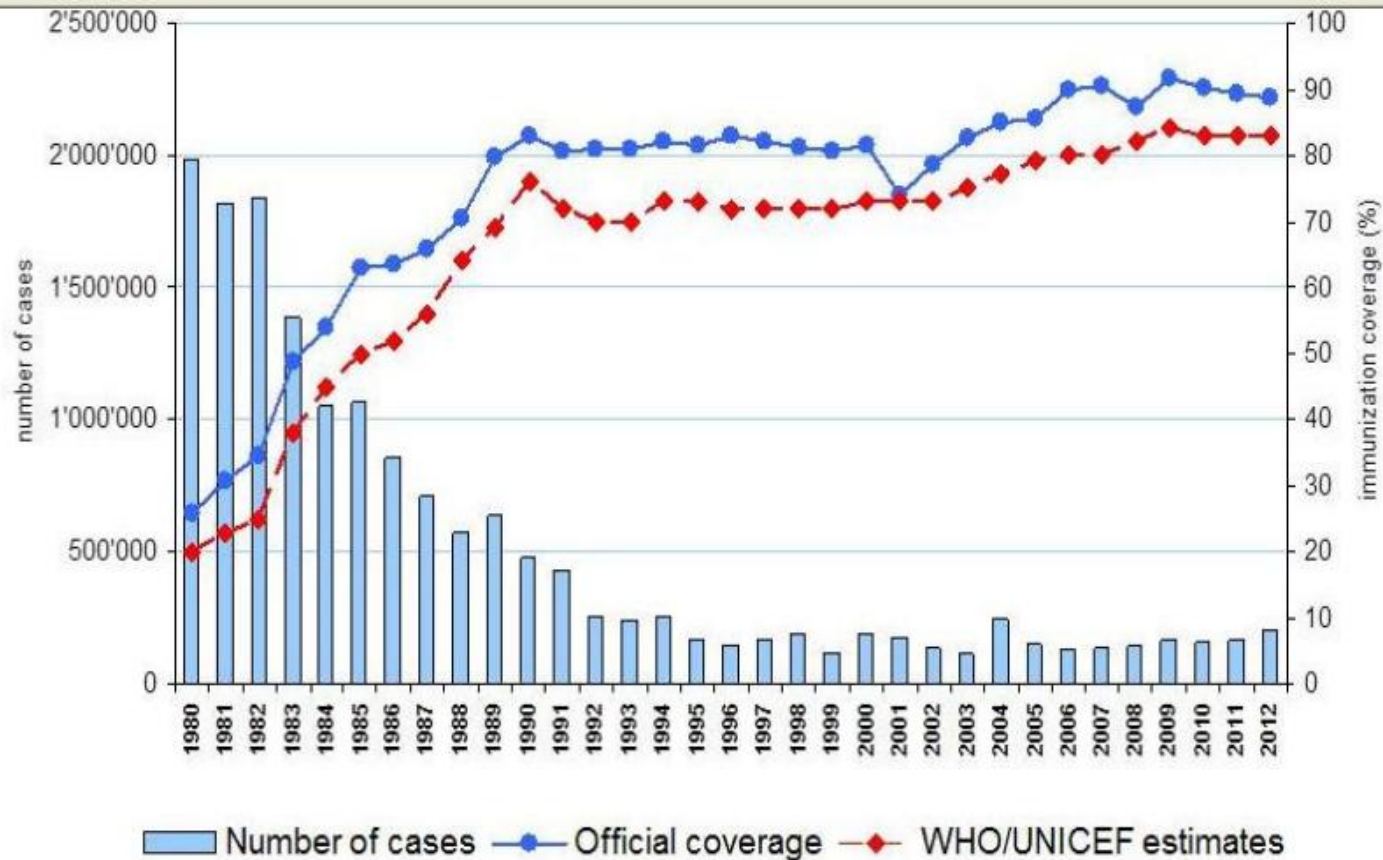
Newborns are too young to be protected by currently available vaccination schedules²

- Pertussis disease are highest in the period between **birth** and **6–8 weeks** of age³
- **76%** of pertussis related deaths occur in infants aged under **2 months**⁴
- **About 90%** of pertussis-related deaths in infants **<6 months old**⁵



1.CDC. In: *Epidemiology and Prevention of Vaccine-Preventable Diseases [Pink Book]*. 2012:215–232 2.Berti E, et al. *Acta Paediatr* 2014;103:846–9.) 3.Meulen et al,*CID*,2016 .4.Healy CM etal *Hum Vac Imm* 5.Grant. In: *Oxford Textbook of Medicine*. 2010: Section 7.6.14

Morbidity of pertussis

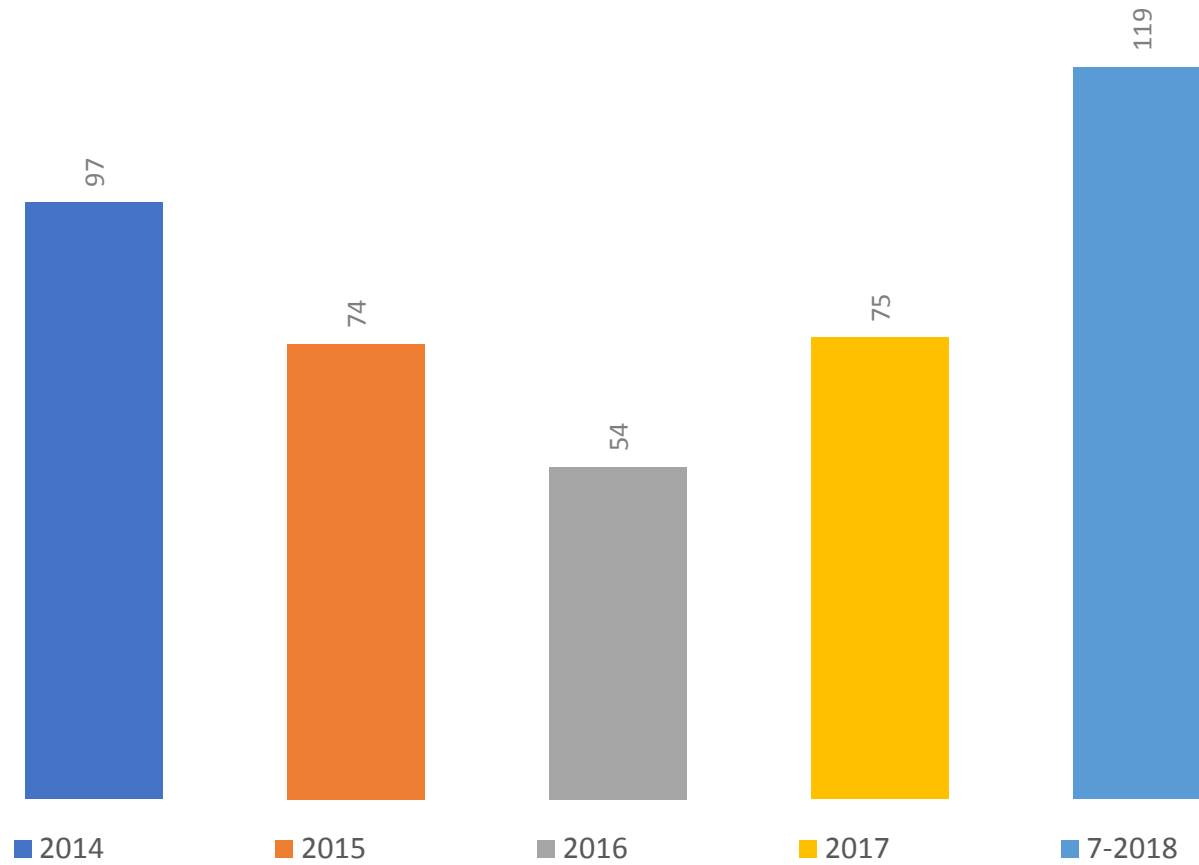


Source: WHO/IVB database, 2013
194 WHO Member States.
Data as of July 2013

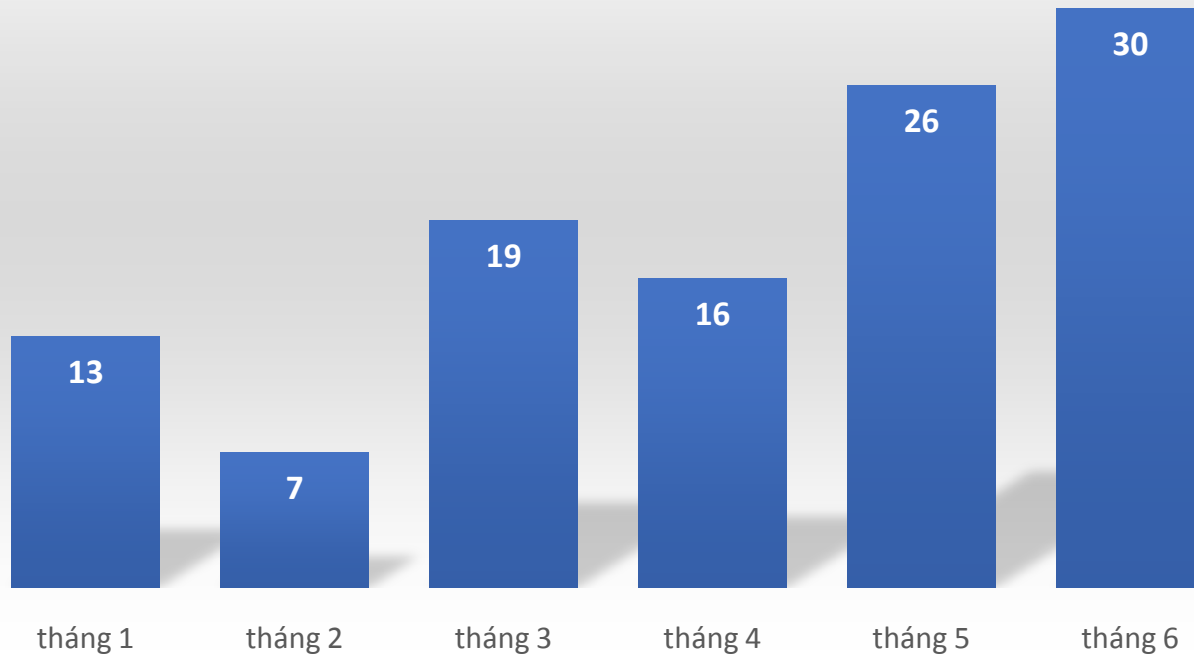
Date of slide: 23 July 2013



HOSPITALIZATION OF PERTUSSIS IN CHILDREN' HOSPITAL 2 FROM 2014-2018



HOSPITALIZATION OF PERTUSSIS IN CHILDREN' HOSPITAL 2 (The first 6 months 2018)



Why are newborn babies vulnerable?

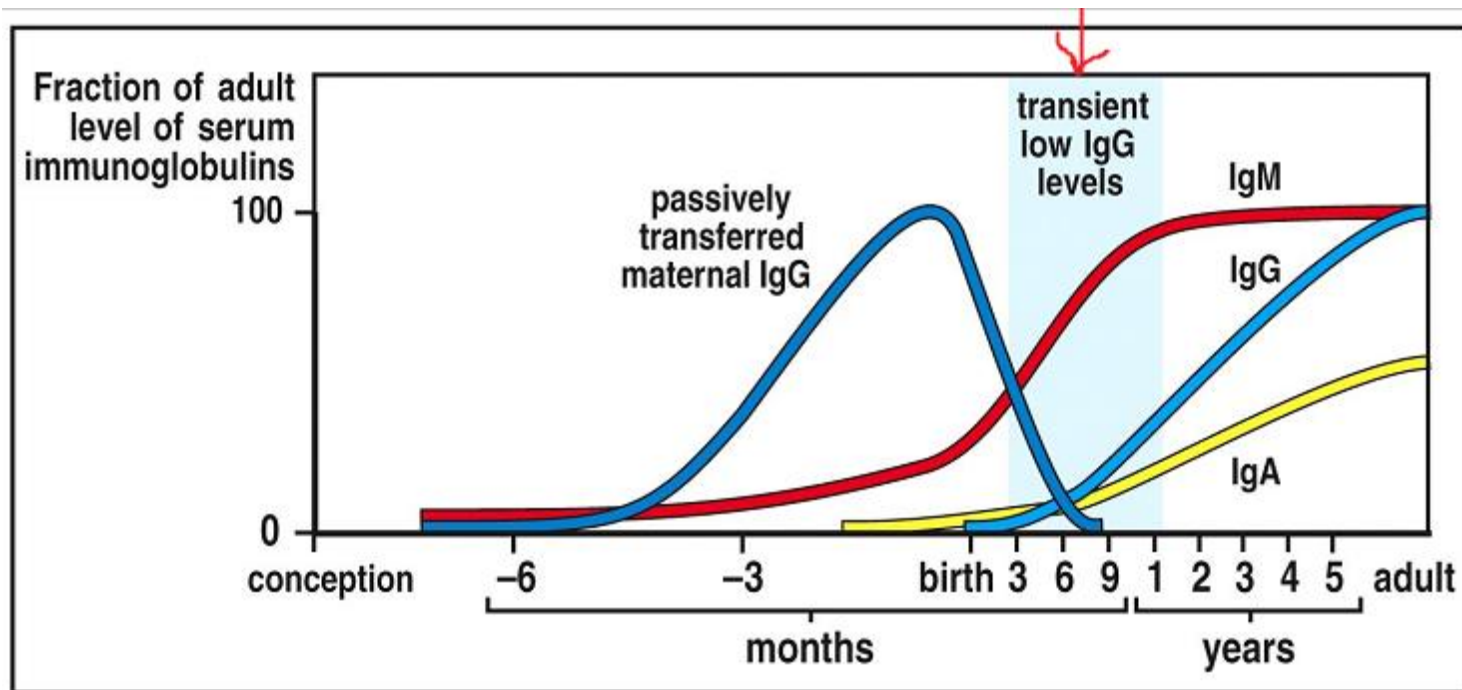
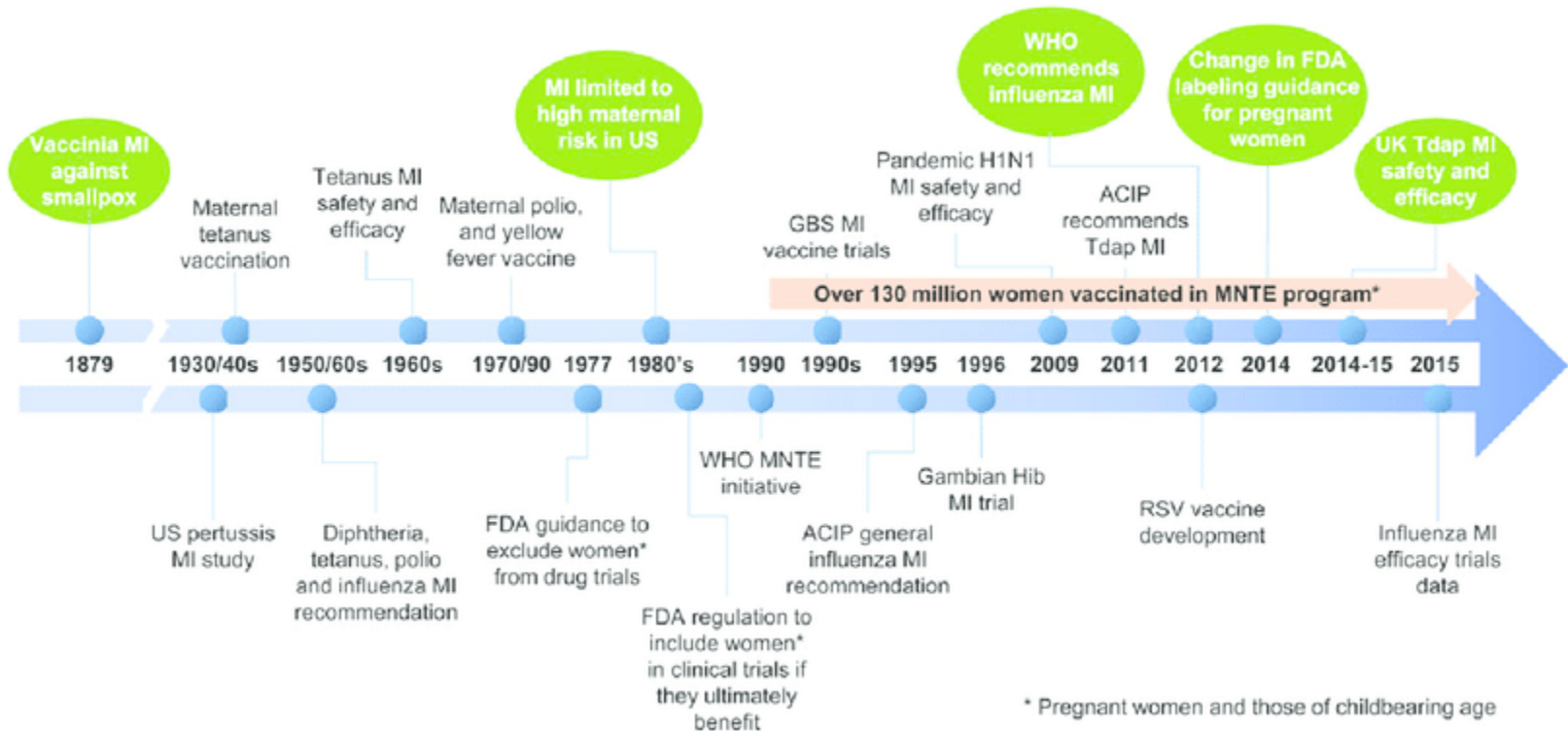


Figure 11-11 Immunobiology, 6/e. (© Garland Science 2005)

The history of maternal immunization



The rate of pertussis vaccination in pregnant women

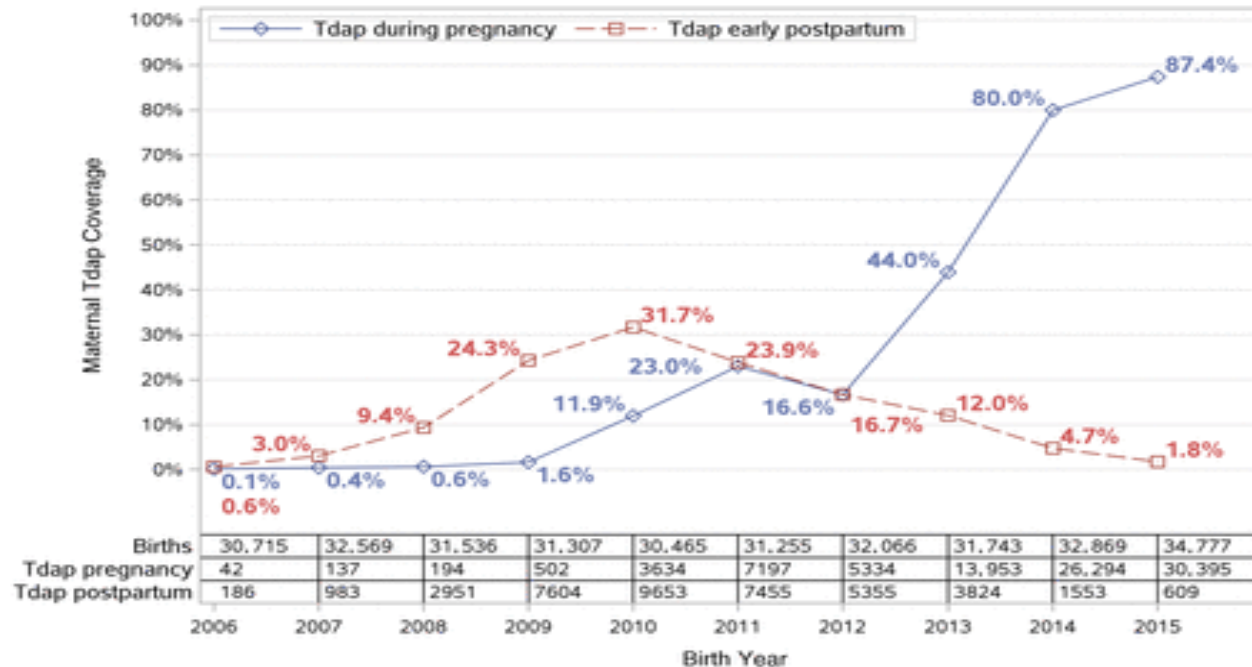


FIGURE 1

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Percentage of infants born in KPNC hospitals whose mother received the Tdap vaccine during pregnancy (at least 8 days before birth) or early postpartum (from the day of birth to 14 days after birth), 2006 to 2015. We include infants whose mothers were continuously enrolled during pregnancy through 14 days postpartum. We exclude the <1% of infants missing data on gestational weeks.

QUESTIONS

1. The effect of Maternal Pertussis vaccination during pregnancy about:
 1. immunogenicity
 2. Reducing the hospitalization rate
2. The safety of Maternal Pertussis vaccination and The optimal time of pertussis vaccination in pregnancy.

immunogenicity

The Effect of Maternal Pertussis Immunization on Infant Vaccine Responses to a Booster Pertussis-Containing Vaccine in Vietnam

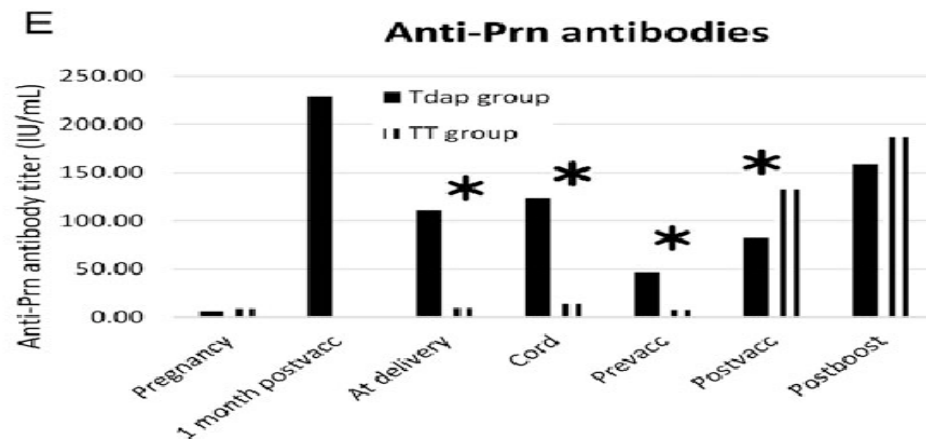
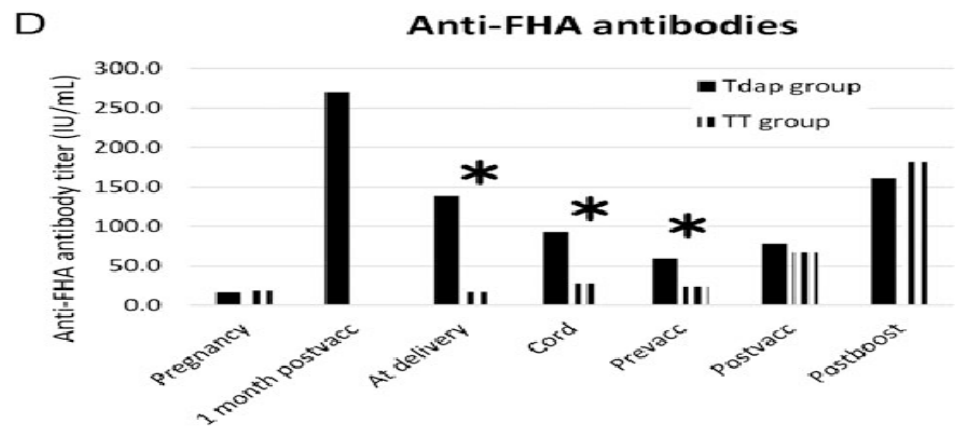
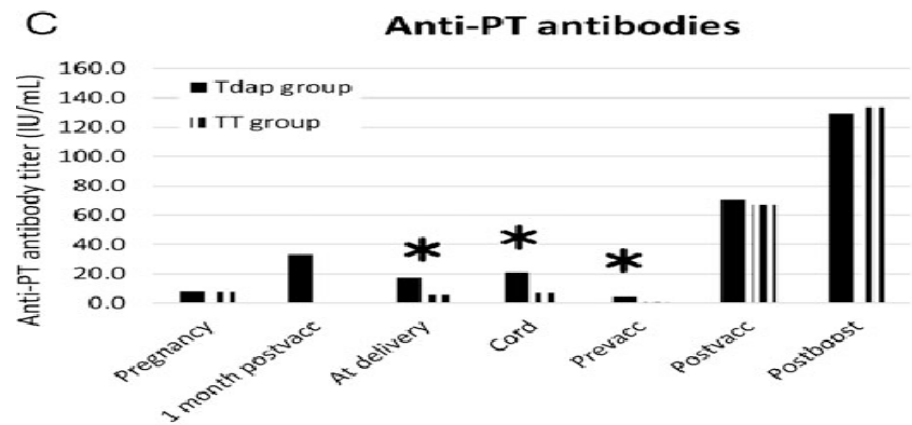
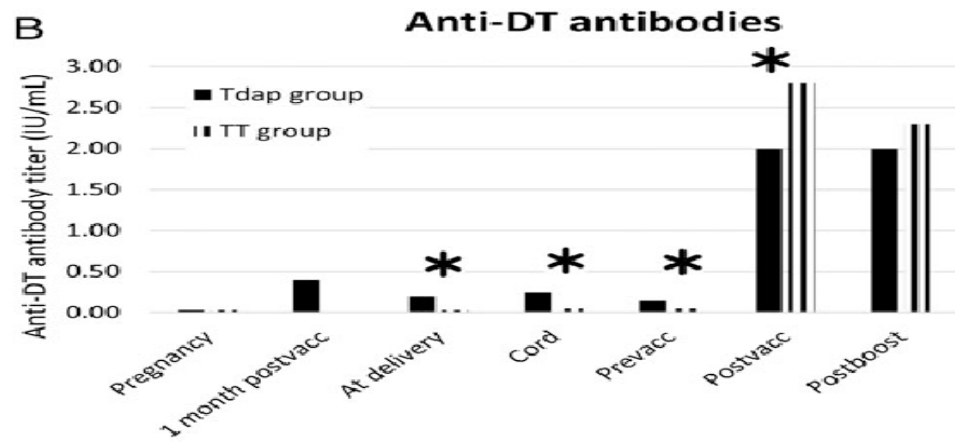
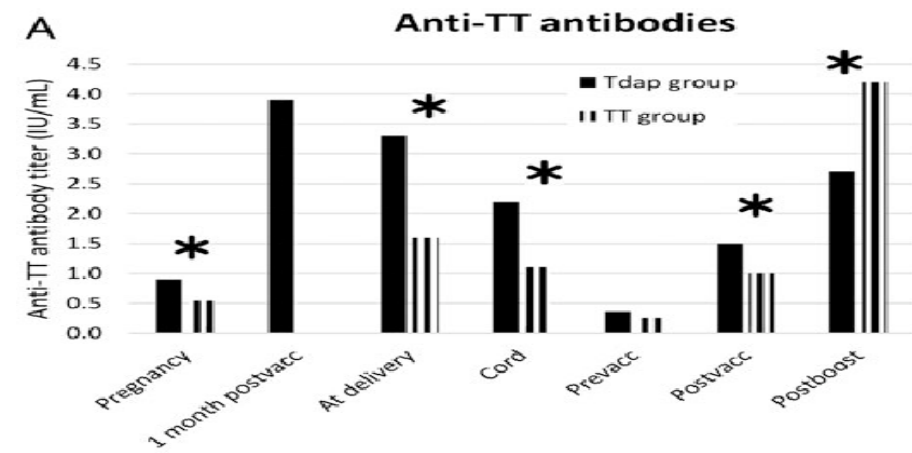
Kirsten Maertens,¹ Thi Thu Ha Hoang,² Trung Dac Nguyen,² Raïssa Nadège Caboré,³ Thi Hong Duong,² Kris Huygen,³ Niel Hens,^{4,5} Pierre Van Damme,¹ Duc Anh Dang,² and Elke Leuridan¹

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Background. Maternal vaccination with an acellular pertussis (aP)-containing vaccine is a recommended strategy in a growing number of industrialized countries, to protect young infants from disease. Little is known on the effect of this strategy in low- and middle-income countries. Following a previous report on the effect of adding a pertussis and diphtheria component to the tetanus vaccination program in pregnant women in Vietnam, we report on infant immune responses to a booster aP vaccine dose in this randomized controlled clinical trial.

Methods. Thirty infants of Tdap (tetanus, diphtheria, and acellular pertussis)-vaccinated pregnant women and 37 infants of women vaccinated with a tetanus-only vaccine received a fourth aP-containing vaccine dose in the second year of life. Blood was taken 1 month after the fourth infant dose. Immunoglobulin G (IgG) antibodies against pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (Prn), tetanus toxoid (TT), and diphtheria toxoid (DT) were measured using commercially available enzyme-linked immunosorbent assays (ELISA).

Results. One month after the booster dose, significantly lower antibody titers were measured in the Tdap group for anti-TT IgG





Efficacy and safety of pertussis vaccination for pregnant women – a systematic review of randomised controlled trials and observational studies

Marie Furuta^{1*} , Jacqueline Sin², Edmond S. W. Ng³ and Kay Wang⁴

Abstract

Background: Worldwide, pertussis remains a major health problem among children. During the recent outbreaks of pertussis, maternal antenatal immunisation was introduced in several industrial countries. This systematic review aimed to synthesize evidence for the efficacy and safety of the pertussis vaccination that was given to pregnant women to protect infants from pertussis infection.

Methods: We searched literature in the Cochrane Central Register of Controlled Trials, Medline, Embase, and OpenGrey between inception of the various databases and 16 May 2016. The search terms included 'pertussis', 'whooping cough', 'pertussis vaccine,' 'tetanus, diphtheria and pertussis vaccines' and 'pregnancy' and 'perinatal'.

Results: We included 15 articles in this review, which represented 12 study populations, involving a total of 203,835 mother-infant pairs from the US, the UK, Belgium, Israel, and Vietnam. Of the included studies, there were two randomised controlled trials (RCTs) and the rest were observational studies. Existing evidence suggests that vaccinations administered during 19–37 weeks of gestation are associated with significantly increased antibody levels in the blood of both mothers and their newborns at birth compared to placebo or no vaccination. However, there is a lack of robust evidence to suggest whether these increased antibodies can also reduce the incidence of pertussis (one RCT, $n = 48$, no incidence in either group) and pertussis-related severe complications (one observational study) or mortality (no study) in infants. Meanwhile, there is no evidence of increased risk of serious complications such as stillbirth (e.g. one RCT, $n = 103$, $RR = 0$, meaning no case in the vaccine group), or preterm birth (two RCTs, $n = 151$, $RR = 0.86$, $95\%CI: 0.14–5.21$) related to administration of the vaccine during pregnancy.

Table 2 Geometric mean concentrations of pertussis antibodies in maternal and infants' blood at birth

	Study design	Intervention/ exposure type, mean gestational week at vaccination (range)	Com-parator	Maternal blood at birth				Infant cord blood at birth					
				n: Vaccine/ control	Vaccine Geometric mean (95% CI)	Control Geometric mean (95% CI)	Ratio of geometric means (95% CI)	p	n: Vaccine/ control	Vaccine Geometric mean (95% CI)	Control Geometric mean (95% CI)	Ratio of geometric means (95% CI)	p
PT (BU or IU/ml)*													
Munoz [31]	RCT	Tdap – (30–32)	placebo	33/14	51.0 (37.1–70.1)	9.1 (4.6–17.8)	5.6 (3.0–10.5)	<0.001	31/14	68.8 (52.1–90.8)	14.0 (7.3–26.9)	4.9 (2.8–8.7)	<0.001
Hoang [30]	RCT	Tdap 26 (19–35)	TT	51/47	17.3 (13.0–22.0)	5.7 (4.3–7.6)	3.0 (2.1–4.4)	<0.001	50/47	21.0 (16.0–28.0)	7.2 (5.6–9.4)	2.9 (2.0–4.3)	<0.001
Abu Raya [26]	PCS	Tdap – (≥ 20)	no vac.	61/20	16.9 (10.5–27.0)	0.7 (0.3–1.8)	22.8 (8.8–58.7)	<0.001	61/20	17.81 (10.67–29.74)	1.12 (0.41–3.02)	15.9 (5.6–45.1)	<0.001
		(subset (27–36)		51/20	16.4 (9.6–28.0)	0.7 (0.3–1.8)	22.7 (8.1–60.0)	<0.001	51/20	17.3 (9.5–31.5)	1.12 (0.4–3.0)	15.4 (5.0–47.6)	<0.001
		(subset (≥ 37)		7/20	28.1 (12.5–63.4)	0.7 (0.3–1.8)	38.0 (8.2–174.9)	<0.001	7/20	21.12 (7.9–56.2)	1.12 (0.4–3.0)	18.9 (3.3–108.1)	<0.001
Hardy-Fairbanks [33]	PCS	Tdap – (anytime)	no vac.	5/53	14.3 (–)	7.5 (–)	1.9 (–)	–	5/53	33.5 (–)	12.6 (–)	2.7 (–)	–
Maertens [29]	PCS	Tdap 29 (22–33)	no vac.	56/41	31.4 (26.0–38.0)	6.4 (4.3–9.6)	4.9 (3.3–7.3)	<0.001	58/41	100.7 (82.0–123.0)	124 (8.0–19.0)	8.1 (5.3–12.5)	<0.001
Healy [34]	RCS	Tdap 9 (1–29)	before	19/86	10.5 (6.4–17.1)	14.0 (11.1–17.7)	0.8 (0.4–1.3)	0.29	19/86	17.3 (11.1–26.8)	16.7 (13.2–21.0)	1.0 (0.6–1.8)	0.90
Gall [5]	RCS	Tdap – (anytime)	no vac.						52/52	Mean 28.2 (SE 2.8)	Mean 11.01 (SE 1.8)	MD 17.2 (10.7–23.8)	
FHA (EU or IU/ml)													
Munoz [31]	RCT	Tdap – (30–32)	placebo	33/14	184.8 (142.8–239.1)	21.9 (10.9–44.1)	8.4 (4.8–15.0)	<0.001	31/14	234.2 (184.6–297.3)	25.1 (10.5–60.3)	9.3 (4.9–17.6)	<0.001
Hoang [30]	RCT	Tdap 26 (19–35)	TT	49/47	139.0 (109.0–176.0)	17.3 (14.0–21.4)	8.0 (5.8–11.0)	<0.001	49/46	93.0 (65.0–133.0)	27.3 (20.9–36.7)	3.4 (2.2–5.4)	<0.001
Abu Raya [26]	PCS	Tdap – (≥ 20)	no vac.	61/20	187.4 (162.9–215.7)	13.4 (8.9–20.3)	14.0 (10.0–19.4)	<0.001	61/20	190.2 (160.9–224.8)	17.1 (10.2–28.7)	11.1 (7.4–16.6)	<0.001
		(subset (27–36)		51/20	192.0 (165.9–222.3)	13.4 (8.9–20.3)	14.3 (10.2–20.0)	<0.001	51/20	196.7 (163.4–236.9)	17.1 (10.2–28.7)	11.5 (7.5–17.6)	<0.001
		(subset (≥ 37)		7/20	155.8 (109.3–222.2)	13.4 (8.9–20.3)	11.6 (5.7–23.7)	<0.001	7/20	138.0 (97.6–195.2)	17.1 (10.2–28.7)	8.1 (3.3–19.5)	<0.001
Hardy-Fairbanks [33]	PCS	Tdap – (anytime)	no vac.	5/53	32.5 (–)	9.6 (–)	3.4 (–)	–	5/53	66.1 (–)	15.9 (–)	4.2 (–)	–
Maertens [29]	PCS	Tdap 29 (22–33)	no vac.	56/41	107.0 (91.0–126.0)	21.4 (16.6–27.5)	5.0 (3.8–6.6)	<0.001	58/41	140.0 (109.0–180.0)	27.5 (21.5–35.0)	5.1 (3.6–7.3)	<0.001
Healy [34]	RCS	Tdap 9 (1–29)	before	19/86	49.3 (28.4–85.8)	50.9 (40.6–63.9)	1.0 (0.6–1.7)	0.91	19/86	87.6 (56.3–136.4)	73.0 (57.6–92.6)	1.2 (0.7–2.1)	0.51
Gall [5]	RCS	Tdap – (anytime)	no vac.						52/52	Mean 104.2 (SE 21.7)	Mean 26.8 (SE 4.0)	MD 77.3 (33.6–121.0)	<0.001
PRN (EU or IU/ml)													
Munoz [31]	RCT	Tdap – (30–32)	placebo	45/35	184.5 (110.2–308.8)	12.2 (5.7–28.4)	15.1 (5.9–38.6)	<0.001	35/35	219.0 (134.4–357.0)	14.4 (5.4–38.4)	15.2 (5.9–39.3)	<0.001
Hoang [30]	RCT	Tdap 26 (19–35)	TT	49/48	111.0 (76.0–163.0)	9.4 (6.9–12.5)	11.8 (7.3–19.1)	<0.001	49/47	124 (86–179)	13.9 (10.5–18.2)	8.9 (5.6–14.1)	<0.001
Abu Raya [26]	PCS	Tdap – (≥ 20)	no vac.	61/20	166.0 (125.7–219.4)	8.5 (3.5–20.3)	19.6 (10.0–38.6)	<0.001	61/20	162.1 (120.4–218.2)	10.6 (4.5–25.3)	15.3 (7.6–30.7)	<0.001
		(subset (27–36)		51/20	164.0 (119.5–225.1)	8.5 (3.5–20.3)	19.4 (9.4–39.8)	<0.001	51/20	161.5 (114.7–222.5)	10.6 (4.5–25.3)	15.2 (7.2–32.1)	<0.001
		(subset (≥ 37)		7/20	181.6 (65.5–503.0)	8.5 (3.5–20.3)	21.5 (4.5–101.4)	<0.001	7/20	172.9 (88.7–434.8)	10.6 (4.5–25.3)	16.3 (3.5–75.0)	<0.001
Hardy-Fairbanks [33]	PCS	Tdap – (anytime)	no vac.	5/53	24.4 (–)	6.4 (–)	3.8 (–)	–	5/53	48.5 (–)	8.9 (–)	5.5 (–)	–
Maertens [29]	PCS	Tdap 29 (22–33)	no vac.	57/41	602.0 (485.5–747.0)	18.0 (13.0–24.0)	33.4 (23.4–47.9)	<0.001	57/41	697.0 (573.0–848.0)	21.0 (15.5–28.0)	33.2 (23.7–46.5)	<0.001
Healy [34]	RCS	Tdap 9 (1–29)	before	19/86	40.4 (18.9–87.3)	39.5 (28.3–55.0)	1.0 (0.5–2.2)	0.96	19/86	70 (32.5–150.5)	41.7 (31.6–40.7)	1.2 (0.5–2.6)	0.65
Gall [5]	RCS	Tdap – (anytime)	no vac.						52/52	Mean 333.0 (SE 56.4)	Mean 24.7 (SE 5.8)	MD 308.3 (195.8–420.0)	<0.001

Reducing hospitalization rate



INTERNATIONAL
SOCIETY
FOR INFECTIOUS
DISEASES

Bordetella Pertussis (Bp): impact of Tdap maternal immunization strategy in a pediatric hospital in Argentina. 2003-2016

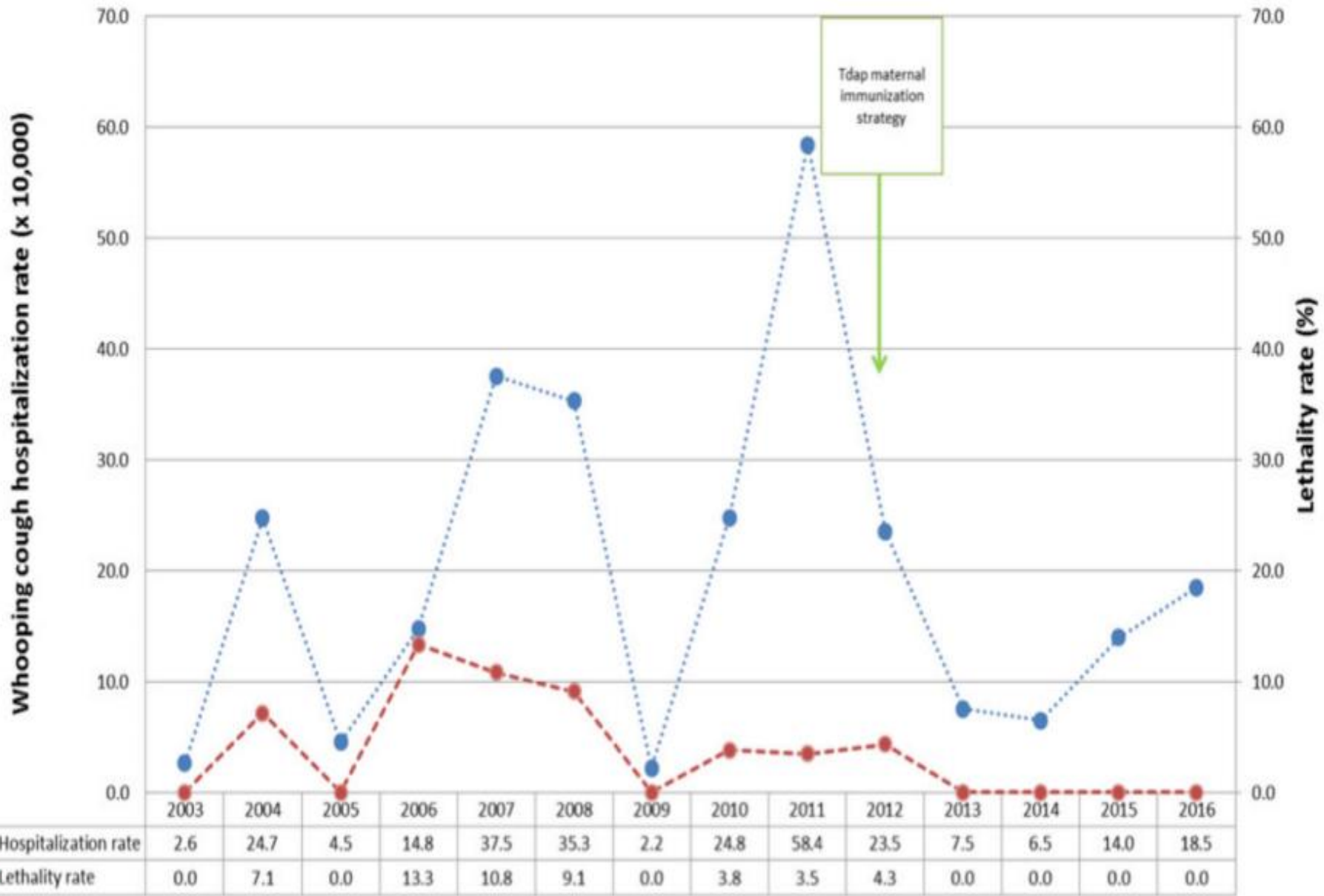
Poster No.: UMP.268

Congress: 18th ICID

Type: Scientific Poster

Authors: M. F. Lucion¹, M. D. V. Juarez¹, M. S. Areso¹, A. C. Martínez¹, V. Romanin¹, M. E. Acevedo², A. Mistchenko², A. Gentile¹; ¹Buenos

Bp hospitalization rate (x10.000) and lethality rate (%). 2003-2016. HNRG.



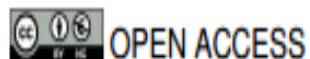
Conclusion

- Confirmed cases were mostly healthy infants younger than 1 year old who had not completed their primary immunization schedule.
- In PostV Bp cases were older and there was a significant decrease in the hospitalization rate.
- There were no fatal cases in our centre after this intervention.

The safety

RESEARCH

Safety of pertussis vaccination in pregnant women in UK: observational study



OPEN ACCESS

Katherine Donegan *pharmacoepidemiologist*, Bridget King *scientific assessor*, Phil Bryan *scientific assessor*

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Objective To examine the safety of pertussis vaccination in pregnancy.

Design Observational cohort study.

Setting The UK Clinical Practice Research Datalink.

Participants 20 074 pregnant women with a median age of 30 who received the pertussis vaccine and a matched historical unvaccinated control group.

Main outcome measure Adverse events identified from clinical diagnoses during pregnancy, with additional data from the matched child record identified through mother-child linkage. The primary event of interest was stillbirth (intrauterine death after 24 weeks' gestation).

Results There was no evidence of an increased risk of stillbirth in the 14 days immediately after vaccination (incidence rate ratio 0.69, 95% confidence interval 0.23 to 1.62) or later in pregnancy (0.85, 0.44 to 1.61) compared with historical national rates. Compared with a matched historical cohort of unvaccinated pregnant women, there was no evidence that vaccination accelerated the time to delivery (hazard ratio 1.00, 0.97 to 1.02). Furthermore, there was no evidence of an increased risk of stillbirth, maternal or neonatal death, pre-eclampsia or eclampsia, haemorrhage, fetal distress, uterine rupture, placenta or vasa praevia, caesarean delivery, low birth weight, or neonatal renal failure, all serious events that can occur naturally in pregnancy.

Conclusion In women given pertussis vaccination in the third trimester, there is no evidence of an increased risk of any of an extensive predefined list of adverse events related to pregnancy. In particular, there was no evidence of an increased risk of stillbirth. Given the recent increases in the rate of pertussis infection and morbidity and mortality in neonates, these early data provide initial evidence for evaluating the safety of the vaccine in pregnancy for health professionals and the public and can help to inform vaccination policy making.

Table

Table 1| Results of matched cohort analyses of safety of pertussis vaccination in pregnant women. Overall risk of predefined potential adverse events in vaccinated women and all women eligible for vaccination versus historical unvaccinated controls

Event*	Vaccinated v historical unvaccinated controls			All eligible women v unvaccinated controls		
	No (%) events			No (%) events		
	Vaccinated women (n=6185)	Matched unvaccinated women (n=18 523)	Incidence rate ratio (95% CI)	Potentially vaccinated women (n=9735)	Matched unvaccinated women (n=29 165)	Incidence rate ratio (95% CI)
Stillbirth	12 (0.19)	42 (0.23)	0.85 (0.45 to 1.61)	25 (0.26)	61 (0.21)	1.21 (0.76 to 1.92)
Neonatal death (within 7 days)	2 (0.03)	6 (0.03)	1.00 (0.20 to 4.95)	2 (0.02)	6 (0.02)	1.00 (0.20 to 4.95)
Pre-eclampsia/eclampsia	22 (0.36)	54 (0.29)	1.22 (0.74 to 2.01)	34 (0.34)	196 (0.67)	0.52 (0.36 to 0.79)
Placenta praevia	2 (0.03)	15 (0.08)	0.40 (0.09 to 1.75)	4 (0.04)	23 (0.08)	0.52 (0.18 to 1.51)
Intrauterine growth retardation/low birth weight/weight <2500 g	126 (2.04)	311 (1.68)	1.20 (0.98 to 1.48)	217 (2.23)	563 (1.93)	1.15 (0.98 to 1.40)
Caesarean section	1238 (20.02)	3748 (20.22)	0.99 (0.93 to 1.06)	1879 (19.30)	5797 (19.88)	0.97 (0.92 to 1.02)
Premature labour (without delivery)	5 (0.08)	21 (0.11)	0.71 (0.27 to 1.89)	10 (0.10)	16 (0.05)	1.88 (0.85 to 4.13)
Postpartum haemorrhage	59 (0.95)	181 (0.98)	0.98 (0.73 to 1.31)	83 (0.85)	312 (1.07)	0.80 (0.63 to 1.01)

*Recorded clinical diagnosis unless specified.

What is the optimal time in pregnancy for the mother to get a pertussis vaccine booster?

You need the whooping cough vaccine during *each* of your pregnancies

The Centers for Disease Control and Prevention (CDC) recommends that pregnant women receive the whooping cough vaccine for adolescents and adults (called Tdap vaccine) during the third trimester of *each* pregnancy. The recommended time to get the shot is during your 27th through 36th week of pregnancy, preferably during the earlier part of this time period. This replaces the original recommendation that pregnant women get the vaccine only if they had not previously received it.

The American College of Obstetricians and Gynecologists (ACOG) makes the following recommendations:

- Obstetric care providers should administer the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine to all pregnant patients during each pregnancy, as early in the 27-36-weeks-of-gestation window as possible.

Efficacy and safety of pertussis vaccination for pregnant women - a systematic review of randomised controlled trials and observational studies.

Furuta M¹, Sin J², Ng ESW³, Wang K⁴.

⊕ Author information

Abstract

BACKGROUND: Worldwide, pertussis remains a major health problem among children. During the recent outbreaks of pertussis, maternal antenatal immunisation was introduced in several industrial countries. This systematic review aimed to synthesize evidence for the efficacy and safety of the pertussis vaccination that was given to pregnant women to protect infants from pertussis infection.

METHODS: We searched literature in the Cochrane Central Register of Controlled Trials, Medline, Embase, and OpenGrey between inception of the various databases and 16 May 2016. The search terms included 'pertussis', 'whooping cough', 'pertussis vaccine,' 'tetanus, diphtheria and pertussis vaccines' and 'pregnancy' and 'perinatal'.

RESULTS: We included 15 articles in this review, which represented 12 study populations, involving a total of 203,835 mother-infant pairs from the US, the UK, Belgium, Israel, and Vietnam. Of the included studies, there were two randomised controlled trials (RCTs) and the rest were observational studies. Existing evidence suggests that vaccinations administered during 19-37 weeks of gestation are associated with significantly increased antibody levels in the blood of both mothers and their newborns at birth compared to placebo or no vaccination. However, there is a lack of robust evidence to suggest whether these increased antibodies can also reduce the incidence of pertussis (one RCT, n = 48, no incidence in either group) and pertussis-related severe complications (one observational study) or mortality (no study) in infants. Meanwhile, there is no evidence of increased risk of serious complications such as stillbirth (e.g. one RCT, n = 103, RR = 0, meaning no case in the vaccine group), or preterm birth (two RCTs, n = 151, RR = 0.86, 95%CI: 0.14-5.21) related to administration of the vaccine during pregnancy.

CONCLUSION: Given that pertussis infection is increasing in many countries and that newborn babies are at greatest risk of developing severe complications from pertussis, maternal vaccination in the later stages of pregnancy should continue to be supported while further research should fill knowledge gaps and strengthen evidence of its efficacy and safety.

Conclusion

- Pertussis vaccination during pregnancy closes adequately the susceptibility of gap for infection in young unvaccinated infants.
- The effect and safety of maternal pertussis immunization in infant are obvious.
- The optimal time of pertussis vaccination in pregnancy is between 27-36 weeks of gestation

Thank you for your attention

